REMARKS

Claim Amendments

Entry of the present amendment and reconsideration of this Application is respectfully requested. The withdrawn claims 21 to 24, 48 to 50, 61, 64, 68 to 70, 83, and 85 to 87 have been canceled. Applicants expressly reserve the right to prosecute these claims, or claims based on the same subject matter, in other applications, such as continuation applications. Claim 18 is amended herein and claims 88-92 are newly added. The claim amendment and new claims are fully supported by the specification and claims as filed and do not introduced new matter. Their entry is respectfully requested. After entry of the present amendment, claims 18, 71-82, 84, and 88-92 are pending in the application and under examination.

Support for the amendment to claim 18 and for new claims 88 and 89, which dependent form claim 18, can be found in the original claim 24 as filed, and, for example, in Figures 3, 4, and 5A-5C, which exemplify the detectable binding pattern from a fluorescently labeled antigen on an antibody array. Support can also be found in paragraph 67 of the specification which defines the term "detectably labeled," paragraph 68 on substances suitable for labeling proteins, and paragraph 71 directed to protein expression profiles of cells.

Support for the new claim 90 and dependent claims 91-92, can be found in the paragraphs, figures and examples discussed above for claims 18, 88 and 89. Additional support can be found in the original claim 28 as filed, and in Examples III and VI which discuss scanning of the microarrays.

Regarding Information Disclosure Statement

An Information Disclosure Statement accompanies this response.

I. Claim Rejections under 35 U.S.C. §103(a)

Brott et al. (PNAS 88:755-759, (1991)) Piehler et al. (SPIE 2504: 185-194, (1995))

Claims 18 and 71 are rejected under 35 U.S.C. §103(a) as being obvious over Brott et al in view of Piehler et al. The Examiner alleges that it would have been obvious to combine the teachings of Brott et al., which allegedly discloses the evaluation of protein binding patterns (molecular interactions) in cell lysates of GTPase-activating protein (GAP) and two Src Kinases

wherein the protein binding patterns were compared and differential expression of GAP was analyzed, with Piehler et al. which allegedly teaches methods to detect multiple analyte proteins in an antibody array system utilizing a plurality of cross-reacting antibody species to selectively generate binding patterns.

Regarding obviousness, the U.S. Supreme Court recently clarified the legal standard by citing text from an earlier opinion: "Under § 103, scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." KSR Intern. Co. v. Teleflex Inc., U.S. 2007 (2007 WL 1237837 (U.S.), at 6, citing Graham v. John Deere Co. of Kansas City, 86 S.Ct. 684. Furthermore, the Supreme Court clarified that a teaching away may be an indication of non-obviousness. K.S.R v. Teleflex at 18 citing United States v. Adams, 383 U.S. 39, 40 (1966)). Finally, the Supreme Court clarified that unexpected results support a conclusion of non-obviousness. Id.

Regarding a motivation to combine prior art references, the Supreme Court stated that an Examiner's analysis must be made explicit. Id. at 13. Furthermore, the Supreme Court noted that it can be important to identify a reason to combine elements from different references. Id. The Supreme Court warned that "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning." Id. at 16, citing Graham, 393 U.S., at 36.

Brott et al. is directed to examination of molecular interactions between GAP and the two Src kinases by forming immunoprecipitates of Src or GAP prepared from cell lysates, wherein the proteins from the immunoprecipitates are resolved by gel electrophoresis and analyzed by an immunoblot procedure with antibodies to GAP or Src used as probes. Thus, Brott et al. teach a method wherein immune complexes are formed in solution by contacting anti-Src antibodies with a lysate and purified on Protein A-Sepharose; then the immune complexes are analyzed by immunoblot analysis with an anti-GAP antibody (see "Cell Lysis and Protein Analysis" section beginning on page 755). As conceded in the Office Action, Brott et al. is silent as to the use of microarrays. However, Brott et al. has an additional deficiency: Brott et al. does not disclose

contacting antibodies on any solid surface with a cell lysate to generate a binding pattern. In Brott et al. as indicated above, the cell lysate is contacted with an antibody in solution, not on a solid support, to form immunoprecipitates, not to generate a binding pattern.

Piehler et al et al., in combination with Brott et al., does not overcome the deficiencies **of** Brott et al. First, although Piehler et al. mentions "arrays," this reference does not disclose microarrays. The paper discloses coating the wells of microtiter plates with a single antibody in each well, and apparently coating a surface in a flow cell with a single antibody in each flow cell, neither of which are microarrays. Furthermore, like Brott et al., Piehler et al. does not disclose contacting antibodies on any solid surface with a cell lysate to generate a binding pattern. In fact, the only solid support of Brott et al. that one could conceivably swap out for the flow cell method of Piehler et al., is the immunoblot membrane, which is not contacted by a cell lysate.

Despite the fact that the invention claimed in the previously pending claims recites elements that are not disclosed in the combination of Brott et al. and Piehler et al., to expedite issuance of the present case, the Applicants have added the recitation that the first cell lysate comprises antigens coupled to a first fluorescent dye and the second cell lysate comprises antigens coupled to a second fluorescent dye. Accordingly, the combination of the teachings of Brott *et al.* with the teachings of Piehler *et al.* does not render the instantly claimed invention obvious. Accordingly, Applicants respectfully request that the rejection be withdrawn.

II: Claim rejections under 35 U.S.C. § 103(a)

Brott et al. (PNAS 88:755-759, (1991)) Piehler et al. (SPIE 2504: 185-194, (1995)) and Ekins et al. (Clin. Chem. 37: 1955-1967, (1991))

Claims 72-75, 77, and 80-82 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over Brott et al in view of Piehler et al. and further in view of Ekins et al. The examiner notes that Brott et al. and Piehler et al. differ from the instant invention in not specifically teaching multiple antigens and antibody preparations. The Examiner alleges that "Ekins et al. teach method to detect proteins via multianalyte microspot immunoassay.

Ekins et al. is not enabling and does not overcome the deficiencies of Brott et al in view of Piehler et al. Ekins et al. present a theoretical analysis of antibody-antigen binding, without experimental support. There is no data in Ekins et al. to support that the methods disclosed therein work. Furthermore, Ekins et al. concede that there theoretical conclusions are contrary to

currently accepted immunoassay rules ("Because of past confusion regarding the concepts of precision , sensitivity, accuracy, etc., several erroneous concepts have become incorporated within currently accepted rules of immunoassay design. In particular, much higher antibody concentrations are customarily used than are necessary to achieve very high assay sensitivity…" (emphasis added), see 2nd paragraph page 1966.) Accordingly, Ekins et al. does not provide an enabling disclosure that is properly combined with the other cited art.

Even if it were enabling, Ekins et al. does not overcome the deficiencies of Brott et al in view of Piehler et al. Ekins et al. does not disclose contacting antibodies on any solid surface with a cell lysate to generate a binding pattern. Finally, there is no disclosure in Ekins et al. of a first cell lysate that includes antigens coupled to a first fluorescent dye and a second cell lysate that includes antigens coupled to a second fluorescent dye.

Therefore, the combination of the teachings of Brott *et al.* in view of the teachings of Piehler *et al.* and further in view of the teachings of Ekins *et al.* does not render obvious the inventions of claim 72, or claims 73-75, 77, and 80-82, which depend therefrom. Applicants assert that claims 72-75, 77, and 80-82 are nonobvious under 35 U.S.C. §103(a) over the cited art, and Applicants respectfully request that the rejection be withdrawn.

III: Claim rejections under 35 U.S.C. § 103(a)

Brott et al. (PNAS 88:755-759, (1991)) Piehler et al. (SPIE 2504: 185-194, (1995) and Cupo (J. Chromatography 569: 389-400 (1991))

Claims 76, 78-79, and 84 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over Brott et al in view of Piehler et al. and further in view of Cupo. The examiner notes that Brott et al. and Piehler et al. differ from the instant invention in not teaching protein expression pattern evaluation in cancer diseases or virus cell lines (like T cells). It is alleged that Cupo provides this teaching in that allegedly "Cupo teaches a two dimensional polyacrylamide gel electrophoresis procedures to measure matrix proteins. The protein are tissue-type specific and can reflect changes in the state of differentiation of a cell."

Cupo does not overcome the deficiencies of Brott et al in view of Piehler et al. Cupo does not disclose contacting antibodies on any solid surface with a cell lysate to generate a binding pattern. Furthermore, there is no disclosure in Cupo of a first cell lysate that includes antigens coupled to a first fluorescent dye and a second cell lysate that includes antigens coupled to a

second fluorescent dye. Therefore, the combination of the teachings of Brott *et al.* with the teachings of Piehler *et al.* and further with the teachings of Cupo does not render obvious the inventions of claims 76, 78-79, and 84, which depend from Claim 18, and Applicants respectfully request that the rejection be withdrawn.

Conclusion

Applicants respectfully assert that upon entry of the present Amendment, the pending application is now in condition for allowance. Prompt and favorable consideration of this Amendment and Reply is therefore respectfully requested.

Respectfully submitted,

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